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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/551,380	04/18/2000	Donald Choy Chang	MLY-5	2514

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EXAMINER

FRONDA, CHRISTIAN L

ART UNIT PAPER NUMBER

1652

DATE MAILED: 02/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/551,380

Applicant(s)

CHANG ET AL.

Examiner

Christian L Fronda

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7,25,26,28,30-34 and 36 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4,6,7,25,26,28,30-34 and 36 is/are rejected.
- 7) ☒ Claim(s) 5 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 April 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____.  |

Art Unit: 1652

### DETAILED ACTION

1. Claims 1-7, 25, 26, 28, 30-34, and 36 are under consideration in this Office Action. Rejections stated in the previous Office Action have been withdrawn in favor of new rejections and new grounds of rejection which are stated in the instant Office Action.

#### *Claim Rejections - 35 U.S.C. § 112, 1st Paragraph*

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-4, 6, 7, 25, 26, 28, 30-34, and 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4, 6, 7, 25, and 26 are genus claims that are directed toward any fluorescent protein of any amino acid sequence and structure comprising any protease cleavage site of any amino acid sequence and structure, wherein proteolytic cleavage at said cleavage site causes alteration of any one of emission and excitation spectra of said fluorescent protein.

The scope of the claims 1-4, 6, 7, 25, and 26 includes many fluorescent proteins from many biological sources, where the fluorescent proteins have widely differing structural, chemical, and physical characteristics. Furthermore, the claimed genus is highly variable because a significant number of structural differences between genus members is permitted.

The disclosed green fluorescent protein mutant of GFP(S65T) having amino acid sequence of SEQ ID NO: 41 is not representative of the entire scope of the claimed genus; but rather is only representative of a genetically engineered green fluorescent protein comprising a caspase cleavage cite, wherein the said genetically engineered green fluorescent protein comprises the amino acid sequence of SEQ ID NO: 41.

The specification also fails to describe additional representative members of these fluorescent proteins by any identifying structural characteristics or properties for which no predictability of structure is apparent. Given this lack of additional representative members as encompassed by the claimed genus, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize

Art Unit: 1652

Applicants were in possession of the claimed invention.

Claims 28, 30-34, and 36 are genus claims that are directed toward any fluorescent protein of any amino acid sequence and structure including the recited loops and beta sheets comprising any protease cleavage site of any amino acid sequence and structure, wherein proteolytic cleavage at said cleavage site causes alteration of any one of emission and excitation spectra of said fluorescent protein.

The scope of the claims 28, 30-34, and 36 includes many fluorescent proteins from many biological sources, where the fluorescent proteins have widely differing structural, chemical, and physical characteristics. Furthermore, the claimed genus is highly variable because a significant number of structural differences between genus members is permitted.

The disclosed green fluorescent protein mutant of GFP(S65T) having amino acid sequence of SEQ ID NO: 41 is not representative of the entire scope of the claimed genus; but rather is only representative of a genetically engineered green fluorescent protein comprising a caspase cleavage site incorporated into a loop structure, wherein the said genetically engineered green fluorescent protein comprises the amino acid sequence of SEQ ID NO: 41.

The specification also fails to describe additional representative members of these fluorescent proteins by any identifying structural characteristics or properties for which no predictability of structure is apparent. Given this lack of additional representative members as encompassed by the claimed genus, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Amending the claims to recite the specific amino acid sequence (SEQ ID NO) of the fluorescent protein may overcome this rejection.

### ***Claim Rejections - 35 U.S.C. § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 2, 25, 26, 28, 29, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Xu et al. This reference was attached to the previous Office Action dated

Art Unit: 1652

10/24/2001 (Paper No. 10).

Applicant's arguments filed 11/04/2002 have been fully considered but they are not persuasive. Applicant's argue that the claimed invention is directed toward an inserted cleavage site within a single fluorescent protein molecule. The Examiner disagrees for reasons of record as supplemented below.

Xu et al. teach the construction of a genetically engineered fluorescent protein, where a green fluorescent protein (GFP) is linked by an 18 amino acid peptide containing the caspase-3 (CPP32) cleavage site, DEVD, to blue fluorescent protein (BFP), wherein cleavage at the cleavage site results in alteration of at least one of the emission and excitation spectra (see entire publication and Figure 2). The GFP taught by Xu et al. is expected to be an 11-stranded  $\beta$ -barrel with a coaxial  $\alpha$ -helix, with the chromophore forming from the central helix as indicated by the Ormo et al. reference stated in the specification on page 10, 1st paragraph, and that the cleavage site is positioned according to the recited positions in the claims.

The genetically engineered fluorescent protein taught by Xu et al. is deemed to be a single fluorescent protein since the GFP and BFP are covalently linked together by a short peptide to form a single, continuous polypeptide having a single, continuous amino acid sequence, where the polypeptide has a caspase cleavage site inserted in it. Thus, the reference teachings anticipate the claimed invention.

### ***Conclusion***

6. No claim is allowed.

7. Claim 5 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.


8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Friday between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura N Achutamurthy can be reached on (571)272-0928. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

9. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

Art Unit: 1652

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLF



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